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CASE REPORT

# Gigantism and hyperprolactinemia in polyostotic fibrous dysplasia (Mc Cune - Albright syndrome)

C. Polychronakos, G. Tsoukas, J.R. Ducharme, J. Letarte, and R. Collu
Division of Endocrinology, Pediatric Research Center, Ste-Justine Hospital, University of Montreal, 3175 Ste - Catherine Road, H3T 1C5 Montreal, Quebec, Canada

**ABSTRACT. A case of Mc Cune-Albright syndrome is presented with the unusual combination of gigantism and hyperprolactinemia. Dynamic exploration of the endocrine functions suggests the presence of an autonomous pituitary adenoma as the cause of the abnormal hormonal findings. These were successfully normalized by radiotherapy to the pituitary gland.**

## INTRODUCTION

Hyperfunction of almost every endocrine gland has been reported in association with the Mc Cune-Albright syndrome, in addition to the precocious puberty which, along with the fibrous dysplasia of the bones and the irregular pigmented spots, define the syndrome.
Several cases of growth hormone (GH) hypersecretion have been reported (1-3) as well as one case of hyperprolactinemia (4) and an abnormal hypothalamic function has been suggested as the cause for the hormonal findings (5). This report will describe the first case, to our knowledge, of hypersecretion of both GH and prolactin (PRL) as well as laboratory findings which are in favor of an autonomous pituitary hyperfunction.

## MATERIALS AND METHODS

*Case Report.* The patient is a boy now aged 14 9/12 years. Beginning at the age of 3 years, he sustained multiple pathological fractures. Since the age of 4, the parents had noticed an accelerated rate of growth and facial asymmetry. When first seen by us, at age 9 11/12 years, he measured 150 cm (4 SD above mean for age) and had a bone age of 12 6/12 years. He had many irregular hyperpigmented spots and his genitalia were at Tanner stage II. Multiple lesions of fibrous dysplasia were evident at radiologic examination. Skull lesions caused a preponderance of facial bones on the right side with ipsilateral exophthalmus and optic atrophy.

*Key-words:* Mc Cune-Albright, prolactin, growth hormone, gigantism.

*Correspondence:* R. Collu, M.D., Division of Endocrinology, Pediatric Research Center, Ste-Justine Hospital, 3175 Ste-Catherine Road, Montreal, Quebec, Canada H3T 1C5.

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The results of the endocrine workup are summarized in Table 1.
Basal levels of GH and PRL were abnormally elevated, 23 to 50 and 27 to 86 ng/ml respectively, and increased (paradoxically for GH) with TRH.
L-dopa failed to suppress PRL but somewhat decreased GH levels. Somatostatin (GHRIH) infusion (200 μg/kg/h) had no appreciable effects on GH values and a paradoxical GH rise to the oral glucose tolerance test (OGTT) was observed. The luteinizing hormone (LH) showed a prepubertal response to LH-RH infusion, possibly as a consequence of the high PRL levels. Exploration of the hypothalamo-pituitary-thyroid and hypothalamo-pituitary-adrenal axes gave normal results. The volume of the sella turcica was normal but there was a slight asymmetry attributable to lesions of the sphenoidal bone.
In the following 8 months the patient grew at a rate of 15 cm/year (Fig. 1). Extensive reconstructive surgery was performed to decompress the optic nerves and improve facial appearance. At 11 years of age, bromocriptine, 2.5 mg bid was started because of continuous rapid rate of growth. Over the next 6 months growth velocity dropped to 5 cm/year while puberty progressed with appearance of pubic and axillary hair. Bromocriptine was then increased to 2.5 mg t.i.d. The patient was lost to follow-up for the following year. During this time he had a minor epileptic seizure investigated in another hospital. Bromocriptine was stopped and diphenylhydantoin, 100 mg t.i.d., was started. He was seen again by us at age 13 years. He had grown at a rate of 12 cm during the previous year and was at Tanner III pubertal stage. Basal GH was 18 ng/ml and PRL 76 ng/ml. Bromocriptine, 2.5 mg t.i.d. was resumed. Under treatment hormone levels remained elevated and their response to TRH unchanged (Table 1). The height velocity could not be assessed during the 6 month of therapy as the height had actually slightly

Table 1 - *Hormonal profile of the patient before treatment and during bromocriptine treatment.*

| | Before treatment | | | | | | | | | On Bromocriptine | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | TRH 100 μg | | | OGTT 1.75 g/kg | GHRIH 200 μg/kg/h | L-DOPA 500 mg | | LH-RH 100 μg/3 h | | TRH 100 μg | |
| Time min. | GH ng/ml | PRL ng/ml | TSH μU/ml | GH ng/ml | GH ng/ml | GH ng/ml | PRL ng/ml | FSH ng/ml LER-907 | LH ng/ml LER-907 | GH ng/ml | PRL ng/ml |
| - 10 | 43 | 86 | 4.8 | | 38.5 | 29 | 28 | 71 | 14 | 54 | 37 |
| 0 | 49 | 84 | 8.3 | 50 | 50 | 23 | 27 | 100 | 12.5 | 65 | 35 |
| 10 | 71 | 122 | 9.4 | | | 14 | 31 | | | 72 | 55 |
| 30 | 74 | 124 | 16.4 | 70 | 43 | 21 | 29 | 100 | 14 | 72 | 54 |
| 60 | 38 | | 10.7 | 38 | | 15 | 27 | 242 | 31 | 83 | 39 |
| 90 | | | 8.2 | | 33 | 13 | 24 | 291 | 30 | 67 | 37 |
| 120 | 90 | 102 | 6.6 | 90 | 40 | 19 | 24 | 206 | 28 | 69 | 36 |
| 180 | | | | | | | | 459 | 32 | | |
| Normal pubertal response | [1] | [3] 10-25 ng/ml | [3] 10-20 μU/ml | [2] | [2] | [3] 7-33 ng/ml | [2] | [3] 2-6 X baseline | [3] 5-20 X baseline | | |
| Normal baseline | <10 ng/ml | <17 ng/ml | <10 μU/ml | | | | | 50-250 ng/ml | 25-60 ng/ml | | |

[1] = no response; [2] = decrease; [3] = increase.

NOM: _____ NO DOSSIER: _____

DATE DE NAISSANCE: _____

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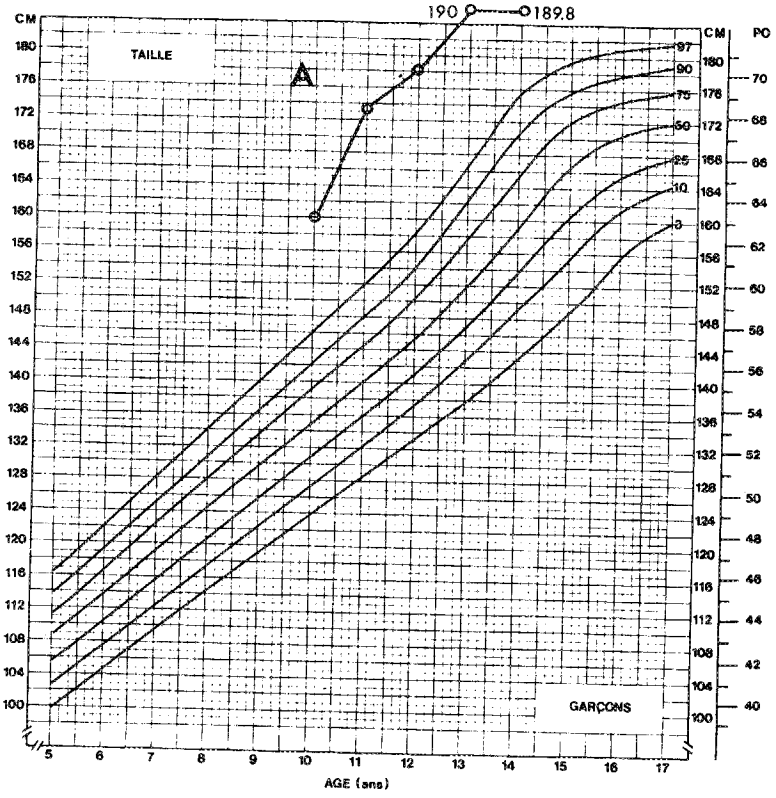


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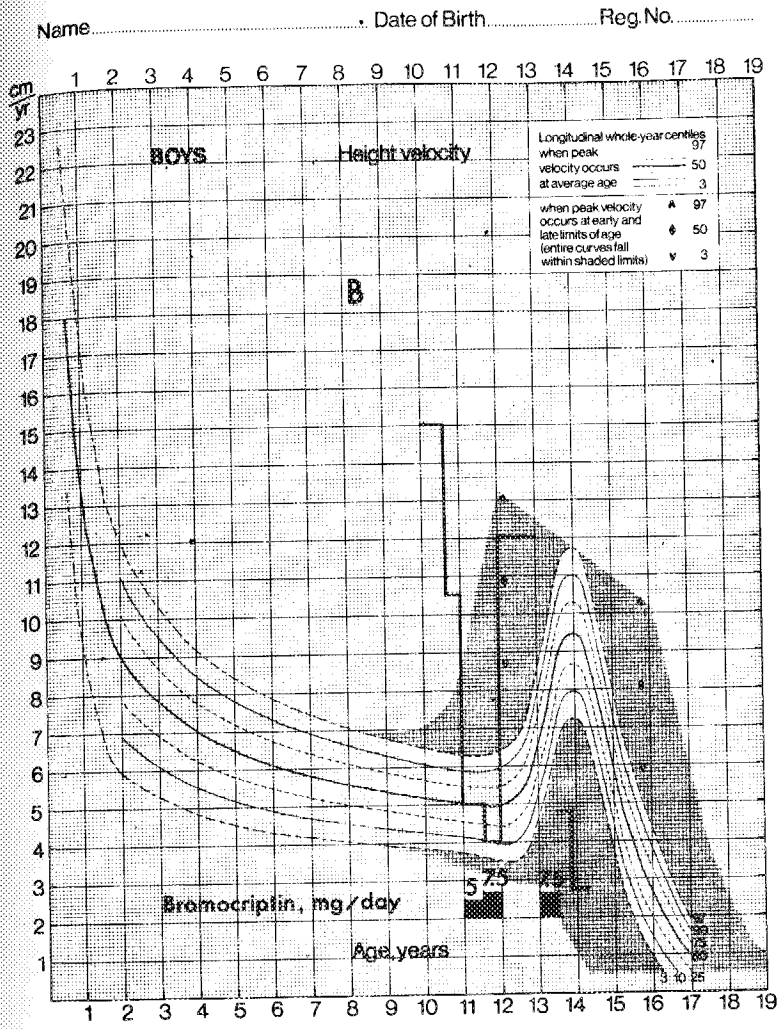
Fig. 1 - *A, growth curve, and B, growth velocity of the patient. Duration and dose of bromocriptine therapy are shown in panel B.*

| | On Bromocriptine | |
|---|---|---|
| g/3 h | TRH 100 μg | |
| H ng/ml ER-907 | GH ng/ml | PRL ng/ml |
| 14 | 54 | 37 |
| 12.5 | 65 | 35 |
| | 72 | 55 |
| 14 | 72 | 54 |
| 31 | 83 | 39 |
| 30 | 67 | 37 |
| 28 | 69 | 36 |
| 32 | | |
| 5-20 X aseline | | |
| 25-60 g/ml | | |




decreased because of developing femoral deformities. Because of poor compliance, bromocriptine was stopped at age 13 6/12 years and the patient received radiotherapy (5,000 rads) to the pituitary. Three months later, the growth velocity was assessed at 4.8 cm/year. Basal GH and PRL values were 30 and 35 ng/ml, respectively.

At the latest follow-up visit, 9 months post radiotherapy, he was growing at a rate of 2.8 cm/year and was at Tanner IV pubertal stage. Basal GH and PRL levels had dropped to 5.5 and 5 ng/ml respectively.

## DISCUSSION

The mechanism of the endocrine abnormalities in the Mc Cune-Albright syndrome remains unknown, but evidence summarized by Di George (6) would favor autonomous hyperfunction of the pheripheral glands. It is not clear, however, whether the pituitary adenomata reported are primary or secondary to hypothalamic dysfunction.

In the present report, the paradoxical increase of GH levels following TRH and decrease with L-DOPA might indicate hypothalamic dysfunction. However, we were unable to show a suppression of PRL by L-DOPA or of GH by somatostatin, which would be clearly in favor of an autonomous pituitary adenoma. In a recent study (7) 66% of acromegalic patients were found to have elevated basal PRL levels.

From the therapeutic point of view, bromocriptine seems to have been effective in reducing the growth rate although hormonal values remained unchanged. This dopaminergic drug has been used successfully for the treatment of PRL-secreting adenomas (8) but its usefulness in acromegaly is doubtful (9). Both boys with gigantism previously reported (1, 2) developed expansive intrasellar lesions. These considerations, along with poor compliance to medication, prompted us to opt for the radiotherapy. A surgical approach was thought to be impossible because of deformities of the bones surrounding the pituitary fossa. Radiotherapy

*ve, and B, growth velocity n and dose of bromocrip- vn in panel B.*

was clearly effective in reducing both the growth rate and plasma hormone levels.

In summary, we have presented a case of Mc Cune-Albright syndrome with the unusual combination of gigantism and hyperprolactinemia which showed a good response to radiotherapy. An autonomous pituitary adenoma is favored by our data as the cause of the abnormal hormonal findings.

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